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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/731,741	12/10/2003	Thomas M. Schmitt	2223-171	5362

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EXAMINER	
SINGH, ANOOP KUMAR	
ART UNIT	**PAPER NUMBER**
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/731,741	SCHMITT ET AL.	
	Examiner	Art Unit	
	Anoop Singh	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12,13,17,22 and 50-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *22,52 and 53* is/are allowed.

6)☒ Claim(s) *12,13,17,50 and 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Finality of the previous office action of August 8, 2007 has been withdrawn and the prosecution on the merit has been reopened in view of new art rejections.

The amendments to the claims filed on October 23, 2007 have been entered. Claims 1-11, 14-16, 18-21, 23-49 have been canceled, while claims 12 and 22 have been amended. Applicants have also added new claims 50-53 that are generally directed to the elected subject matter. Claims 12, 13, 17, 22, 50-53 are pending and under current examination.

Election/Restrictions

Applicant's response to the Restriction was received on 12/20/2004. Applicants elected the subject matter of group I, drawn to a method of forming cells of the T cell lineage. Claims 18-21, 23, and 25-28 were withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 1-17, 22 and 24 were examined, while the examiner in the interests of compact prosecution rejoined claim 22.

Withdrawn-Claim Rejections - 35 USC § 112

Claims 12-13, 17 and 22 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of amendments to the claim clarifying the term "an *in vitro* system".

Withdrawn-Claim Rejections - 35 USC § 103

Claims 1, 2 and 4 rejected under 35 U.S.C. 103(a) as being unpatentable over Jaleco et al (2001, J. Exp. Med. 194:991-1001, IDS), Nakano et al. (1994, Science 265:5175 IDS) and Tatsumi et al. (1990, Proc. Natl. Acad. Sci. 87:2750-2754, IDS) is overcome by cancellation of claims 1, 2 and 4. However, upon further consideration a new art is applied to pending claims 12-13 and 17 as presented below.

New-Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 12-13, 17, 50 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jaleco et al (2001, J. Exp. Med. 194:991-1001, IDS), Nakano et al. (1994, Science 265:5175 IDS), Pui et al (Immunity. 1999, 11(3):299-308) and Tatsumi et al. (1990, Proc. Natl. Acad. Sci. 87:2750-2754, IDS).

Jaleco et al. provides guidance on a method of using an *in vitro* system comprising stromal cells the Delta-1 ligand, which supports T cell lymphopoiesis of human hematopoietic progenitor cells (HPCs) but does not support B cell lymphopoiesis (Abstract). Specifically, Jaleco et al. teaches that culturing HPCs with mouse S-17 stromal cells that express Delta-1 inhibits B cell differentiation and produces CD3+ CD4+CD8+ T cells (pg. 992, Materials and Methods; pg. 995, Table 1). Abbas et al. teaches that T cells that are CD3+ CD4+CD8+ have inherently undergone TCR V(D)J rearrangement {Abbas et al., (1994) Cellular and Molecular Immunology 2nd ed., 1-457; pg. 176, Fig. 8-5; pg.178 col. 1}. Jaleco et al teaches that transfecting S-17 stromal cells specifically blocks B cell lymphopoiesis

(Abstract). Further, Jaleco et al. teaches that the immature T cells were separated from the aggregate population of cells (pg. 995, Table 1). Jaleco et al. does not teach using OP-9 stromal cells or inducing lymphopoiesis in mouse cells.

Nakano et al. supplements the guidance of Jaleco et al. by teaching the use of mouse OP-9 stromal cells (which inherently does not express M-CSF) to generate lymphohematopoietic cells (Abstract). Nakano et al. teaches that it is advantageous to use stromal cells lacking M-CSF when studying lymphopoiesis because the presence of M-CSF can inhibit the differentiation of ES cells to blood cells other than macrophages. However, Nakano et al do not teach transfecting OP-9 cells.

However, prior to instant invention, Pui provided guidance with respect to constitutive expression of activated Notch1 resulting in the emergence of a population of thymic-independent T cells in the bone marrow, concurrent with an early and persistent block in B cell maturation. Pui et al also disclose that constitutive Notch1 signaling did not affect myeloid maturation (see abstract and page 300, col. 1, para. 1 and page 300, col. 2, para. 1). However, Pui do not teach transfecting OP-9 cells with Notch liagands..

Tatsumi supplements the guidance of Jaleco et al. by teaching an *in vitro* system for studying the differentiation of mature mouse T cells from CD3- CD4- CD8- precursors by culturing them with mouse stromal cells (Abstract; pg. 2750, Materials and Methods). However, Tatsumi et al do not teach culturing OP-9 cells.

Accordingly, based on the guidance provided by Jaleco et al. on a method of using an *in vitro* system comprising stromal cells the Delta-1 ligand, which supports T cell lymphopoiesis of HPCs but does not support B cell lymphopoiesis and the teachings of Nakano et al. on the advantages of using OP-9 cells when studying lymphopoiesis, it would be *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to try modifying the teachings of Jaleco et al. by replacing the mouse S-17 stromal cells with OP-9 cells with reasonable expectation of achieving predictable result. It would have been obvious for one of

ordinary skill in the art to try particularly since Pui et al taught expression of activated Notch1 would result in the emergence of a population of thymic-independent T cells in the bone marrow, concurrent with an early and persistent block in B cell maturation. Thus given that Jaleco taught a method of forming T cell using an in vitro system using another mouse stromal cell and use of mouse OP-9 stromal cells that inherently does not express M-CSF) to generate lymphohematopoietic cells (Abstract) were available and known at the time of filing of this application, it would be *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to try using the assay system of Jaleco et al. with the OP-9 cells of Nakano et al to study mouse T cell differentiation with the mouse precursor cells using the precursors taught by Tatsumi et al and Pui in order to reduce the number of inhibitory ligands and to optimize T cell induction and variety of sub-types induced.

One who would practiced the invention would have had reasonable expectation of success because modifying the teachings of Jaleco et al. by replacing the S-17 stromal cells with the OP-9 cells of Nakano et al. would have been a routine modification in the art at the time of filing, particularly in view of teaching of Nakano et al and Pui. In addition, use of mouse hematopoietic precursor cells, such as those taught by Tatsumi et al instead of human hematopoietic precursors would have been a routine modification in the art at the time of filing. Thus, it would have only required routine experimentation to modify the method disclosed by Jaleco to include OP-9 cells for forming T cell linage as required by instant invention.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

Claims 12, 13, 17, 50-51 are rejected, while Claims 22, 52-53 are allowable.

The following is a statement of reasons for the indication of allowable subject matter: Claims 22, 52 and 53 are not included in the 103(a) rejection since claims require differentiation of stem or progenitor cells to form T cells of specific lineage which is increased by at least about 10 to 15 fold that is not disclosed in prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anoop Singh whose telephone number is (571) 272-3306. The examiner can normally be reached on 9:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272- 4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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